U.S. Department of Commerce Atty. Docket No. Serial No. 67780/JPW/AJM/NS|10/764,068 Patent and Trademark Office Applicant INFORMATION DISCLOSURE STATEMENT Rene Hen et al. (Use several sheets if necessary) Filing Date Group January 22, 2004 U.S. PATENT DOCUMENTS Examiner Document Number Date Name Class Subclass Filing Date Initial if Appropriate FOREIGN PATENT DOCUMENTS Document Number Date Country Class Subclass Translation Yes No OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) Aberg, M. A., Aberg, N. D., Hedbacker, H., Oscarsson, J., and Eriksson, P. S. (2000). Peripheral infusion of IGF-I selectively induces neurogenesis in the adult rat hippocampus. J Neurosci 20, 2896-903; (Exhibit 1) Altman, J. (1962). Are new neurons formed in the brains of adult mammals? Science 135, 1127-1128; (Exhibit 2) Altman, J., and Das, G. D. (1965). Autoradiographic and histological evidence of postnatal hippocampal neurogenesis in rats. J Comp Neurol 124, 319-335; (Exhibit 3)

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DK		Bannerman, D. M., Deacon, R. M., Offen, and Rawlins, J. N. (2002). Double dissociation hippocampus: spatial memory and hyponeo 884-901; (Exhibit 5)	lation of function phagia. Behav Ne	n within the urosci 116,			
DIL		Benraiss, A., Chmielnicki, E., Lerner, K., Roh, D., and Goldman, S. A. (2001). Adenoviral brain-derived neurotrophic factor induces both neostriatal and olfactory neuronal recruitment from endogenous progenitor cells in the adult forebrain. J Neurosci 21, 6718-31; (Exhibit 6)					
DK	7	Blanchard, R. J., and Blanchard, D. C. (1969). Crouching as an index of fear. J Comp Physiol Psychol 67, 370-5; (Exhibit 7)					
DK	8.	Blanchard, R. J., and Blanchard, D. C. (reactions to fear-eliciting stimuli. J C 129-35; (Exhibit 8)					
DK	9	Blier, P., and de Montigny, C. (1994). Cu the treatment of depression. Trends Pharm 9)	irrent advances anacol Sci 15, 220	nd trends in -6; (Exhibit			
DK		Bodnoff, S. R., Suranyi-Cadotte, B., Ait Meaney, M. J. (1988). The effects of chro in an animal model of anxiety. Psych (Exhibit 10)	onic antidepressa	nt treatment			
· DK		Bodnoff, S. R., Suranyi-Cadotte, B., Quirion, R., and Meaney, M. J. (1989). A comparison of the effects of diazepam versus several typical and atypical anti-depressant drugs in an animal model of anxiety. Psychopharmacology 97, 277-9; (Exhibit 11)					
7K		Bremner, J. D., Randall, P., Vermetten, F. Mazure, C., Capelli, S., McCarthy, G., I. S. (1997). Magnetic resonance imaging-base volume in posttraumatic stress disorder rand sexual abusea preliminary report. (Exhibit 12)	nnis, R. B., and ed measurement of related to childho	Charney, D. hippocampal ood physical			
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G., Rajkowska, G., Du, F., Seraji- 2000). Enhancement of hippocampal chem 75, 1729-34; (Exhibit 14)	Bozorgzad, N., an neurogenesis by	nd Manji, H lithium
, J. F., Markou, A., and Luc epressant activity in rodents: rec . Trends Pharmacol Sci 23, 238-45;	ent developments (Exhibit 15)	and future
B., Michaelis, T., Watanabe, T., Fr n, M., Bartolomucci, A., and Fuchs es in cerebral metabolites, hip feration are prevented by anti- ptine. Proc Natl Acad Sci U S A 98,	, E. (2001). Str pocampal volume, depressant trea	ress-induce , and cell tment with
C., and Duman, R. S. (20 plasticity. Bipolar Disord 4, 183-9	02). Antidepres 4; (Exhibit 17)	ssants and
n, R. M., Bannerman, D. M., and Rawli ts of cytotoxic hippocampal lesions ; (Exhibit 18)	in rats. Behav Ne	eurosci 116
ot, A., and Treit, D. (2002). Dors nergic systems modulate anxiety in t . Brain Res <i>949</i> , 60; (Exhibit 19)	sal and ventral he plus-maze and	hippocampa shock-prob
do, P. L., Miller, H. L., Salomon, I , Moreno, F. A., Heninger, G. R., ophan-depletion challenge in depre ramine or fluoxetine: implications : echanism of antidepressant action. oit 20)	and Charney, D. ssed patients to for the role of s Biol Psychiatry	S. (1999) reated with serotonin in 46, 212-20
oit 21)	r zone astrocyte: brain. Cell 97,	s are 703-16;
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))	s. N., Craddock, K. J., Abel, T. mmental enrichment modifies the PK ad improves hippocampus-dependent r it 22) mcc considered, whether or not citation is in conformance	S. N., Craddock, K. J., Abel, T., and Nguyen, P. nmental enrichment modifies the PKA-dependence of dimproves hippocampus-dependent memory. Learn Memory.

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PK		Duman, R. S., Heninger, G. R., and Nestler, E. J. (1997). A molecular and cellular theory of depression. Arch Gen Psychiatry 54, 597-606; (Exhibit 24)			
DK	25	Eichenbaum, H. (1999). The hippocampus: Biol 9, R482-4; (Exhibit 25)	The shock of the new. Curr		
DK	Feng, R., Rampon, C., Tang, Y. P., Shrom, D., Jin, J., Kyin, M., Sopher, B., Miller, M. W., Ware, C. B., Martin, G. M., Kim, S. H., Langdon, R. B., Sisodia, S. S., and Tsien, J. Z. (2001). Deficient neurogenesis in forebrain-specific presentilin-1 knockout mice is associated with reduced clearance of hippocampal memory traces. Neuron 32, 911-26; (Exhibit 26)				
DK		File, S. E., Kenny, P. J., and Cheeta, S. (2000). The role of the dorsal hippocampal serotonergic and cholinergic systems in the modulation of anxiety. Pharmacol Biochem Behav 66, 65-72; (Exhibit 27)			
PK		Frank-Kamenetsky, M., Zhang, X., Bottega, S., Guicherit, O., Wichterle, H., Dudek, H., Bumcort, D., Wang, F., Jones, S., Shulok, J., Rubin, L., and Porter, J. (2002). Small-molecule modulators of Hedgehog signaling: identification and characterization of Smoothened agonists and antagonists. J. Biol. 1:10, 10.1-9; (Exhibit 28)			
-DK		Garcia-Verdugo, J. M., Doetsch, F., Wich Alvarez-Buylla, A. (1998). Architecture subventricular zone: in search of the st 234-48; (Exhibit 29)	and cell types of the adult		
DK	30	Gorman, J. M. (2002). Treatment of gene Clin Psychiatry 63, 17-23; (Exhibit 30)	ralized anxiety disorder. J		
DK	31 Gould, E., and Gross, C. G. (2002). Neurogenesis in adult mammals: some progress and problems. J Neurosci 22, 619-23; (Exhibit 31)				
DK		Gould, E., and Tanapat, P. (1999). Stress and hippocampal neurogenesis. Biol Psychiatry 46, 1472-9; (Exhibit 32)			
DK		Gould, E., Tanapat, P., McEwen, B. S., Flugge, G., and Fuchs, E. (1998). Proliferation of granule cell precursors in the dentate gyrus of adult monkeys is diminished by stress. Proc Natl Acad Sci U S A 95, 3168-71; (Exhibit 33)			
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OTHE	RI	OCCUMENTS (Including Author, Title, Date,	Pertinent Pages, Etc.)		
DK	34	Griebel, G., Simiand, J., Serradeil-Le of M., Scatton, B., Maffrand, J. P., and Sowand antidepressant-like effects of the receptor antagonist, SSR149415, suggest a treatment of stress-related disorders. If 6370-5; (Exhibit 34)	Gal, C., Wagnon, J., Pascal ubrie, P. (2002). Anxiolytic non-peptide vasopressin VII n innovative approach for the Proc Natl Acad Sci U S A 99		
クと		Gross, C., Santarelli, L., Brunner, D (2000). Altered fear circuits in 5-HT(Psychiatry 48, 1157-63; (Exhibit 35)			
DK	36	Gross, C., Zhuang, X., Stark, K., Ramboz Santarelli, L., Beck, S., and Hen, R. acts during development to establish nor the adult. Nature 416, 396-400; (Exhibit	(2002). Serotoninia receptor mal anxiety-like behaviour in		
DK		Gurvits, T. V., Shenton, M. E., Hokama, H., Ohta, H., Lasko, N. B., Gilbertson, M. W., Orr, S. P., Kikinis, R., Jolesz, F. A., McCarley, R. W., and Pitman, R. K. (1996). Magnetic resonance imaging study of hippocampal volume in chronic, combat-related posttraumatic stress disorder. Biol Psychiatry 40, 1091-9; (Exhibit 37)			
DK	38	Hastings, N. B., and Gould, E. (1999). F the CA3 region by adult-generated granul 146-54; (Exhibit 38)	apid extension of axons into le cells. J Comp Neurol 413		
7K	39 Heisler, L. K., Chu, H. M., Brennan, T. J., Danao, J. A., Bajwa, P., Parsons, L. H., and Tecott, L. H. (1998). Elevated anxiety and				
9K	Henze, D. A., Wittner, L., and Buzsaki, G. (2002). Single granule cells reliably discharge targets in the hippocampal CA3 network in vivo. Nat Neurosci 5, 790-5; (Exhibit 40)				
DK	41	Jacobson, L., and Sapolsky, R. (1991). The feedback regulation of the hypothalami axis. Endocr Rev 12, 118-34; (Exhibit 41)	.c- pituitary-adrenocortical		
DIR	42	Kaplan, M. S., and Hinds, J. W. (1977). N electron microscopic analysis of light r 1092-4; (Exhibit 42)	eurogenesis in the adult rat radioautographs. Science 197		
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DK	43	Kempermann, G. (2002). Regulation of adulimplications for novel theories of major (17-33; (Exhibit 43)	lt hippocampal ne depression. Bipol	urogenesis - ar Disord 4,		
DK	44	Kempermann, G., Kuhn, H. G., and Gage, F. on neurogenesis in the dentate gyrus of a U S A 94, 10409-14; (Exhibit 44)	H. (1997). Genet dult mice. Proc N	ic influence atl Acad Sci		
.OK		Kempermann, G., Kuhn, H. G., and Gage, F. neurons in adult mice living in an enric 493-5; (Exhibit 45)	hed environment.	Nature 386,		
δK	46	Kirschenbaum, B., and Goldman, S. neurotrophic factor promotes the survival adult rat forebrain subependymal zone. E 210-4; (Exhibit 46)	of neurons aris	ing from the		
DK		Kopp, C., Vogel, E., and Misslin, R. (emotional behaviour in three inbred st Processes 47, 161-74; (Exhibit 47)	rains of mice.	Behavioural		
DK	48	Kuhn, H. G., Dickinson-Anson, H., and Gagain the dentate gyrus of the adult raneuronal progenitor proliferation. J New 48)	t: age-related	decrease of		
7K		Lai, K., Kaspar, B., Gage, F., and Son hedgehog upregulates adult neural proger and in vivo. Nature Neuroscience Vol.6	itor proliferati No.1, 21-27; (Ex	.on <i>in vitro</i> hibit 49)		
DK DK	50	LeDoux, J. E., Cicchetti, P., Xagorari (1990). The lateral amygdaloid nucleus amygdala in fear conditioning. J Neurosc	s, A., and Roman : sensory interi	nski, L. M. face of the		
DK.		LeDoux, J. E., Sakaguchi, A., and Reis, efferent projections of the medial genic emotional responses conditioned to acous 683-98; (Exhbit 51)	ulate nucleus me tic stimuli. J N	diate eurosci 4,		
PK	52	Liberatore, G. T., Jackson-Lewis, V., Vu Vila, M., McAuliffe, W. G., Dawson, V Przedborski, S. (1999). Inducible nitri dopaminergic neurodegeneration in the MPT Nat Med 5, 1403-9; (Exhibit 52)	<i>J</i> . L., Dawson, c oxide synthase	T. M., and stimulates		
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ОТНЕ	RI	OCCUMENTS (Including Author, Title, Date,	Pertinent Pages	, Etc.)	
DK.		Malberg, J. E., Eisch, A. J., Nestler, E. Chronic antidepressant treatment increas hippocampus. J Neurosci 20, 9104-10; (Ex	ses neurogenesis hibit 53)	in adult rat	
7K	54 Manev, H., Uz, T., Smalheiser, N. R., and Manev, R. (2001). Antidepressants alter cell proliferation in the adult brain in vivo				
DK		Masand, P. S., and Gupta, S. (1999). Sinhibitors: an update. Harv Rev Psychiat	ry 7, 69-84; (Ex	hibit 55)	
9K		McEwen, B. S. (1999). Stress and hippocampal plasticity. Annu Rev Neurosci 22, 105-22; (Exhibit 56)			
DK	57	McNaughton, N. (1997). Cognitive dysfunction resulting from hippocampal hyperactivitya possible cause of anxiety disorder? Pharmacol Biochem Behav 56, 603-11; (Exhibit 57)			
MK		Menard, J., and Treit, D. (2001). The anxiolytic effects of intra- hippocampal midazolam are antagonized by intra-septal L-glutamate. Brain Res 888, 163-166; (Exhibit 58)			
714		9 Moore, G. J., Bebchuk, J. M., Wilds, I. B., Chen, G., Manji, H. K., and Menji, H. K. (2000). Lithium-induced increase in human brain grey matter. Lancet 356, 1241-2; (Exhibit 59)			
7K		Nakagawa, S., Kim, J. E., Lee, R., Malbe C., Zhang, Y. J., Nestler, E. J., and Du of neurogenesis in adult mouse hippoca response element-binding protein. J Neuro	man, R. S. (2002) ampus by cAMP a sci <i>22</i> , 3673-82;	. Regulation nd the cAMI (Exhibit 60)	
DK		Nibuya, M., Morinobu, S., and Duman, R. S. (1995). Regulation of BDNF and trkB mRNA in rat brain by chronic electroconvulsive seizure and antidepressant drug treatments. J Neurosci 15, 7539-47; (Exhibit 61)			
PK	62 Nilsson, M., Perfilieva, E., Johansson, U., Orwar, O., and Eriksson, P. S. (1999). Enriched environment increases neurogenesis in the adult rat dentate gyrus and improves spatial memory. J Neurobiol 39, 569-78; (Exhibit 62)				
VK	63	Page, M. E., Detke, M. J., Dalvi, A., (1999). Serotonergic mediation of the eddesipramine, in the rat forced swimmi (Berl) 147, 162-7; (Exhibit 63)	fects of fluoxet	ine, but not	
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PK		Parks, C. L., Robinson, P. S., Sibille, (1998). Increased anxiety of mice lacking Proc Natl Acad Sci U S A 95, 10734-9; (ng the serotoninlA receptor. Exhibit 64)		
QK.	Pencea, V., Bingaman, K. D., Wiegand, S. J., and Luskin, M. B. (2001). Infusion of brain-derived neurotrophic factor into the lateral ventricle of the adult rat leads to new neurons in the parenchyma of the striatum, septum, thalamus, and hypothalamus. J Neurosci 21, 6706-17; (Exhibit 65)				
DK		Pham, T. M., Soderstrom, S., Winblad, B. Effects of environmental enrichment hippocampal NGF in the non-handled rats (Exhibit 66)	on cognitive function and Behav Brain Res 103, 63-70;		
DK		Phillips, T. J., Hen, R., and Crabbe, J. C. (1999). Complications associated with genetic background effects in research using knockout mice. Psychopharmacology (Berl) 147, 5-7; (Exhibit 67)			
DK	-	Ramboz, S., Oosting, R., Amara, D. A., Kung, H. F., Blier, P., Mendelsohn, M., Mann, J. J., Brunner, D., and Hen, R. (1998). Serotonin receptor 1A knockout: an animal model of anxiety-related disorder. Proc Natl Acad Sci U S A 95, 14476-81; (Exhibit 68)			
DK		Santarelli, L., Gobbi, G., Debs, P. C., Sibille, E. T., Blier, P., Hen, R., and Heath, M. J. (2001). Genetic and pharmacological disruption of neurokinin 1 receptor function decreases anxiety-related behaviors and increases serotonergic function. Proc Natl Acad Sci U S A 98, 1912-7; (Exhibit 69)			
DK	70 Sargent, P. A., Kjaer, K. H., Bench, C. J., Rabiner, E. A., Messa, C., Meyer, J., Gunn, R. N., Grasby, P. M., and Cowen, P. J. (2000). Brain serotoninlA receptor binding measured by positron emission tomography with [11C] WAY-100635: effects of depression and antidepressant treatment. Arch Gen Psychiatry 57, 174-80; (Exhibit 70)				
DK	71	Seki, T., and Arai, Y. (1995). Age-rela cells in the adult dentate gyrus. Neurore	ted production of new granule eport 6, 2479-82; (Exhibit 71)		
7K		Seri, B., Garcia-Verdugo, J. M., McEwen, (2001). Astrocytes give rise to new ne hippocampus. J Neurosci 21, 7153-60; (E	urons in the adult mammalian		
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γ Κ		Cortical grey matter reductions associa chronic unipolar depression. Controlled study. Br J Psychiatry 172, 527-32; (Ext	ted with treatmen magnetic resona nibit 73)	t-resistant nce imagin
DK	·	Sheline, Y. I., Wang, P. W., Gado, M. Vannier, M. W. (1996). Hippocampal a depression. Proc Natl Acad Sci U S A 93,	trophy in recur	rent major
DK		dimethyltryptamine, d-amphetamine Psychopharmacology 78, 368-72; (Exhibit	diazepam, 5-m and food d 75)	ethoxy-N,N- eprivation,
DK		Shirayama, Y., Chen, A. C., Nakagawa, S. R. S. (2002). Brain-derived neur antidepressant effects in behavioral mod 22, 3251-61; (Exhibit 76)	otrophic factor	produces
·DK		Shors, T. J., Miesegaes, G., Beylin, A Gould, E. (2001). Neurogenesis in the formation of trace memories. Nature 410,	adult is invol 372-6; (Exhibit	ved in the
DiC		Snyder, J. S., Kee, N., and Wojtowicz, J neurogenesis on synaptic plasticity in Neurophysiol 85, 2423-31; (Exhibit 78)	the rat dentat	e gyrus.
DK		Stein, M. B., Koverola, C., Hanna, C., T B. (1997). Hippocampal volume in women v abuse. Psychol Med 27, 951-9; (Exhibit T	ictimized by child	
7K		Tada, E., Parent, J. M., Lowenstein, D. Hirradiation causes a prolonged reduction dentate gyrus of adult rats. Neuroscience	in cell prolifera e 99, 33-41; (Ext	ation in the
JK		van Praag, H., Schinder, A. F., Christie D., and Gage, F. H. (2002). Functiona hippocampus. Nature 415, 1030-4; (Exhib	neurogenesis ir t 81)	the adult
7K		Vitolo, O. V., Sant'Angelo, A., Costanzo O., and Shelanski, M. (2002). Amyloid be PKA/CREB pathway and long-term potentia that enhance cAMP signaling. Proc Natl (Exhibit 82)	ta -peptide inhibi tion: Reversibili Acad Sci U S A 99	ition of the ty by drugs , 13217-21
DK	83	Wang, S., Scott, B. W., and Wojtowicz, properties of dentate granule neurons in 42, 248-57; (Exhibit 83)		

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·DK			Williams, B. M., Luo, Y., Ward, C., Redo A., and McCoy, J. G. (2001). Environme spatial memory and hippocampal CREB imm 73, 649-58; (Exhibit 84)	ntal enrichment: unoreactivity. Ph	effects on ysiol Behav	
Pl			Willner, P., Muscat, R., and Papp, M. induced anhedonia: a realistic animal me Biobehav Rev 16, 525-34; (Exhibit 85)	odel of depression	on. Neurosci	
D14	く ぱ		Wong, M. L., and Licinio, J. (2001). Rese to depression. Nat Rev Neurosci 2, 343-5	61; (Exhibit 86)		
DK			Yoshimura, S., Takagi, Y., Harada, J., Waeber, C., Bakowska, J. C., Breakefield (2001). FGF-2 regulation of neurogenesis brain injury. Proc Natl Acad Sci U S A	, X. O., and Mosko s in adult hippod	owitz, M. A. ampus after	
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